UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,923	03/10/2004	Kenneth W. Dobie	RTS-0739US	9182

34138 7590 03/23/2005

COZEN O'CONNOR, P.C.
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
ASHEN, JON BENJAMIN	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/798,923	DOBIE ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-13,15,16,21,24,25 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-13,15,16,21,24,25 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

1. Applicant's response filed 01/04/05 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 10/18/2004 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. The rejection of claims 1-16, 21, 24-25 and 28 under 35 U.S.C. § 112 second paragraph is withdrawn for the reasons set forth below.

3. The rejection of claims 1-9, 13-16, 21, 24-25 and 28 under 35 U.S.C. § 112 first paragraph is withdrawn for the reasons set forth below.

Response to Arguments

4. Applicant's amendments to claim 1, filed 01/04/05, have overcome the outstanding rejection under 35 U.S.C. § 112 second paragraph.

5. Applicant's amendments to claim 1, filed 01/04/05, have overcome the outstanding rejection under 35 U.S.C. § 112 first paragraph.

Claim Rejections - 35 USC § 102

6. The rejection of claims 1-13, 15-16, 21 and 28 under 35 U.S.C. § 102(b) as being anticipated over Acton et al. (U.S. Patent 6, 194,556) is withdrawn for the reasons set forth below.

7. The rejection of claims 1-13, 15-16, 21 and 28 under 35 U.S.C. § 102(e) as being anticipated over Acton et al. (U.S. Patent 6, 610,497) is withdrawn for the reasons set forth below.

Response to Arguments

8. Applicant's amendments to claim 1, filed 01/04/05, have overcome the outstanding rejections under 35 U.S.C. § 102(b) and (e) as being anticipated over Acton et al. (U.S. Patent 6, 194,556) or Acton et al. (U.S. Patent 6, 610,497).

Claim Rejections - 35 USC § 102 or 35 USC § 103

9. The rejection of claims 1-8, 13-16, 21, 24 and 28 under 35 U.S.C. § 102 or 35 U.S.C. § 103 as being anticipated by or obvious over Monia et al. (U.S. Patent 6, 080546) is withdrawn for the reasons set forth below.

Response to Arguments

10. Applicant's amendments to claim 1, filed 01/04/05, have overcome the outstanding rejection under 35 U.S.C. § 102 or 35 U.S.C. § 103 as being anticipated by or obvious over Monia et al. (U.S. Patent 6, 080,546). However, Applicant's amendment of claim 1 has necessitated the following new ground(s) of rejection under 35 U.S.C. 102(e) or 35 USC 103(a) as being anticipated by or obvious over Ward et al. (U.S. Patent 6,165,728) and under 35 U.S.C. § 103(a) as being unpatentable over Acton et al. (U.S. Patent 6, 194,556) and Monia et al. (U.S. Patent 6, 080546).

11. Claims 1-8, 13, 15-16, 21 and 28 are rejected under 35 U.S.C. 102(e) or 35 USC 103(a) as being anticipated by or obvious over Ward et al. (U.S. Patent 6,165,728).

12. The invention as set forth in claims 1-8, 13, 15-16, 21 and 28 is outlined in the prior Office Action. Ward et al. disclose an antisense oligonucleotide that is SEQ ID NO: 19 that is 20 nucleobases in length and 85% complementary to a nucleic acid molecule encoding ACE2 that is specifically hybridizable to the coding region of ACE2 (at positions 1290-1309) wherein said oligonucleotide can be RNA or DNA (col. 5, lines 25-30). SEQ ID NO: 19 of Ward et al. is disclosed as a "gapmer," a chimeric oligonucleotide that comprises 2'-O-methoxyethyl sugar moieties, phosphorothioate backbone modifications and 5-methylcytosine nucleobase modifications (cols. 40-43, Example 15 and Table 1). Monia et al. also disclose kits comprising the antisense compounds of their invention (column 12, 1st full paragraph).

Furthermore, since the prior art antisense compound meets all the structural limitations of the claims, the prior art antisense compound comprises an antisense compound 8-80 nucleobases in length targeted to a nucleic acid molecule encoding ACE2, wherein said compound is at least 85% complementary to a nucleic acid encoding ACE2. Absent evidence to the contrary, the prior art antisense compound of Monia et al. would inhibit expression of ACE2 mRNA. See, for example, MPEP § 2112, which states "[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. 'There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102.' In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

13. Therefore, the instant invention is anticipated or obvious over Ward et al. (U.S. Patent 6,165,728).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1-13, 15-16, 21, 24-25 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Acton et al. (U.S. Patent 6, 194,556) and Monia et al. (U.S. Patent 6, 080546). The invention as set forth in claims 1-13, 15-16, 21, 24-25 and 28 is outlined in the prior Office Action. Acton et al. teach antisense oligonucleotides targeted to ACE2 (column 23, section 4.3.2) and a particular antisense oligonucleotide that is SEQ ID NO: 13 that is 27 nucleobases in length that is 100% complementary to the coding region of human ACE2 (bases 1550-1576). Acton et al. disclose that the

antisense oligonucleotides of their invention can be RNA or DNA oligonucleotides (column 24, lines 25-27) that can be targeted to the coding region of ACE2 (column 24, lines 53-56), that can be chimeric (column 25, line 11; column 26, line 11) that can comprise backbone, sugar moiety and nucleobase modifications to improve, e.g., the stability, hybridization, or solubility of the molecule (column 25, lines 12-16) wherein the backbone modification can be a phosphorothioate internucleoside linkage (column 24, line 67) wherein said oligonucleotide can comprise a 5-methylcytosine (column 25, line 41). Acton et al. disclose kits of their invention that can comprise an antisense oligonucleotide of their invention (column 5, lines 38-44; column 51, lines 19-22, column 64, lines 3-9).

Acton et al. do not teach the specific sugar modification that is a 2'-0-methoxyethyl sugar moiety.

Monia et al. (U.S. Patent 6,080,546) teach antisense oligonucleotides that comprise at least one modified sugar moiety that is a 2'-O-methoxyethyl sugar moiety (see Table 2). Monia et al. teach that, "Modified oligonucleotides may also contain one or more substituted sugar moieties" (col. 7, lines 18-19) and that "A preferred modification includes 2'-methoxyethoxy (2'-O-Ch2Ch2OCH3, also known as 2'-O-(2-methoxyethyl) or 2'-MOE (col. 7, lines 38-41). Monia et al. also teach that in the context of their invention, the term oligonucleotide includes oligonucleotides having naturally occurring nucleobases, sugars and covalent internucleoside (backbone) linkages as well as oligonucleotides having non-naturally occurring portions which function similarly. Such modified or substituted oligonucleotides are often preferred over native forms

because of desirable properties such as, fore example, enhanced cellular uptake, enhanced affinity for nucleic acid target and increase stability in the presence of nucleases (col. 5, lines 22-31). Monia et al. teach that the antisense compounds used in accordance with their invention can be conveniently and routinely made through the well known technique of solid phase synthesis (col. 10, lines 5-8).

It would have been obvious to one of ordinary skill in the art to make an antisense compound 8-80 nucleobases in length targeted to a nucleic acid molecule encoding ACE2 of SEQ ID NO: 4 wherein the compound was at least 85% complementary to said SEQ ID NO: 4 wherein said compound comprised at least one 2'-O-methyoxyethyl sugar moiety, including all the further limitations of the dependent claims rejected herein, because Acton et al. teach an antisense compound 8-80 nucleobases in length targeted to a nucleic acid molecule encoding ACE2 of SEQ ID NO: 4 wherein the compound was at least 85% complementary to said SEQ ID NO: 4 as each of the further limitations that are not the specifically required sugar modification and because Monia et al. teach the preferred desirability, benefits and ease of making antisense oligonucleotides that comprise the specific sugar modification, a 2'-O-methyoxyethyl sugar moiety.

One of ordinary skill in the art would have been motivated to make an antisense compound 8-80 nucleobases in length targeted to a nucleic acid molecule encoding ACE2 of SEQ ID NO: 4 wherein the compound was at least 85% complementary to said SEQ ID NO: 4 wherein said compound comprised at least one 2'-O-methyoxyethyl sugar moiety, including all the further limitations of the dependent claims rejected

herein, because Acton et al. teach such a compound with all limitations except the particular sugar modification and because Monia et al. teach the preferred desirability and routine nature of making the 2'-O-methyoxyethyl sugar modification. The teaching of Monia et al. parallels the teaching of the instant specification in regards to the preferred desirability and routine nature of making 2'-O-methyoxyethyl sugar modifications to antisense oligonucleotides (see for example pg. 12, 2nd full paragraph; pg. 29, 2nd full paragraph and pg. 30, lines 9-11 in particular), indicating that such modifications were well known and widely applied in the art of antisense at least several years before the instant application was filed.

One of ordinary skill in the art would have expected success in making an antisense compound 8-80 nucleobases in length targeted to a nucleic acid molecule encoding ACE2 of SEQ ID NO: 4 wherein the compound was at least 85% complementary to said SEQ ID NO: 4 wherein said compound comprised at least one 2'-O-methyoxyethyl sugar moiety, including all the further limitations of the dependent claims rejected herein, because Acton et al. teach such a compound with all limitations except the particular sugar modification and because Monia et al. teach the preferred desirability and routine nature of making the 2'-O-methyoxyethyl sugar modification.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jba